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ABSTRACT

Research is reviewed on epilepsy and findings summarized in terms of intelligence, relationship between etiology and intelligence, seizure frequency, age of onset, duration, premorbid intelligence, and specific psychological defects, electroencephalography (EEG) and IQ, and learning. Among findings noted are that the widespread belief among educators that children treated with anticonvulsants are handicapped may contribute to lowered expectations in the classrooms, that epileptic students are unstable in performance and exhibit much test re-test variability, that age of onset contributes to a large extent to the individual's ultimate intelligence and that the type of EEG abnormality is correlated with level of intellectual functioning. Features of commonly used anticonvulsant medications are described, and their therapeutic range and adverse reactions are set out in a table. Forty-two references are listed. (CL)

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Epilepsy, Anticonvulsants and Cognitive Functions in School Students

Epilepsy in the general population is approximately .6%. School psychologists could therefore encounter 20 or more students with epilepsy. Most psychometric instruments measure attention, memory, response speed and visuo-perceptual skills. Frequently, drug studies did not address protracted use of medications or effects upon learning. A review of the literature and findings are presented.

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Epilepsy, Anticonvulsants and Cognitive

Functions in School Students

Estimates on the prevalence of epilepsy in the general population of the United States is approximately, (.6%). Obviously, this figure increases proportionately in special education population figures as well as in state facilities for the developmentally disabled. In addition, individuals who sustain closed head injuries are frequently placed on either phenobarbital or dilantin as a prophylactic measure as are infants with febrile convulsions. A school psychologist serving a normal population could encounter 20 or more students who have epilepsy and are taking one or more anticonvulsant medications.

Nearly all psychometric instruments in combination with other techniques employ questions and tasks measuring attention, short-term memory, long-term memory retrieval, psychomotor speed of response, visuo-spatial/visuo-perceptual skills and general comprehension to mention only a few key areas. Drug studies completed on many anticonvulsants did not take into consideration the long term (chronic) use of the medications nor to their specific properties in regard to cortical function and what effect(s) they might have upon learning.

A review of the literature finds a paucity of work generated in this area. What has been accomplished was completed some ten years ago and further follow-up studies do not appear. Articles pertinent to this topic are found in a wide variety of medically oriented journals and brief reports. Few appear in journals typically read by school psychologists. Few others may be found in neuropsychological literature which is quite specific in its readership.

Two anticonvulsants that are frequently used to control generalized tonic-clonic as well as some absences are partially reviewed for their effects upon learning. Phenobarbital has a sedative effect which may last for a short

period of time if kept in the therapeutic range. However, in some children it produces symptoms of irritability, aggression and sometimes produces a "hyperkinetic syndrome" (Ounsted 1955). This is usually comprised of increased gross motor activity, short attention span, distractibility and destructiveness or aggression. Blood levels in excess of 60 mg/ml result in acute or subacute confusional states, ataxia, dysarthria, nystagmus as well as clear evidence of intellectual impairment. It has been reported that severe developmental delay in childhood misinterpreted as a permanent handicap, has been attributed to chronic intoxication with phenobarbital.

Phenytoin (Dilantin) has many long term use (chronic) effects and a level exceeding 20 mg/ml will demonstrate itself by nystagmus, ataxia, lethargy and dysarthria. Glasser (1972) has described a condition of "diphenylhydantoin encephalopathy", associated with an overdose or average oral dosage but with a high blood level that occurs in patients abruptly. Altered mood and affect also accompany this condition. Although (Freeman 1969), reports that discontinuation of treatment with phenytoin may halt intellectual impairment, in many cases actual recovery may not always occur.

Intelligence

Children with epilepsy (including those of at least average over-all intelligence and apparently in good control) do <u>less</u> <u>well</u> educationally than might be expected in view of their basic intellectual abilities (Hartlage and Green, 1972).

Certainly, it appears to be a widespread belief among educators that children treated with anticonvulsants are handicapped and this belief in itself may contribute to the lowered expectations regarding performance in the classroom (Hartlage and Green, 1972).

Keith et al (1955) found that only 20% of the children with epilepsy in their sample scored in the average to above average range on the Stanford-Binet, while 25% scored in the dull normal range and 53% in the retarded range of intelligence. Obviously, the distribution is markedly skewed toward the lower limits. Results of scores with adults is more normally distributed.

Etiology & Intelligence

The classifications of idiopathic or symptomatic have yielded consistently predictable results on intelligence tests. In all studies the idiopathic type performed better than the symptomatic type with a difference in IQ from 4 - 11 points. These differences are maintained in both children and adults. Thus, it is evident that etiology is an important determinant of IQ (Stores 1978).

The question of intellectual impairment in epilepsy is an old one. Some investigators have not observed impairment, others have. The majority of the studies do implicate a rather gradual impairment of abilities. However, these reports used markedly hetereogenous populations many of whom were from long term care institutions. Interestingly, the issue is the fact that epileptics are unstable in performance and exhibit much test, re-test variability. Therefore, caution should be observed in over-generalizing these results.

Seizure Frequency

Brain damaged individuals without epilepsy in Kløve and Mathews (1966) study performed worse than all other groups except the tonic-clonic seizures of known etiology. On the Halstead Reitan Battery the same relationships are observed between idiopathic and symptomatic groups. Kløve and Mathews (1966) found that . . . . it is the injury to the brain which causes impairment in functioning and not the seizure discharge per se.

(Insert Table I about here)

The role of seizure frequency is not clear. The total number of seizures is negatively correlated with IQ. Individuals with absence seizures typically have had the most seizures and most frequently possess the highest IQ as compared to other groups. This observation suggests that though the number of seizures is an important factor to intelligence, it is not as vital as the severity of the seizure itself.

Age of Onset

Age of onset of a seizure disorder contributes to a large extent to the ultimate intelligence level of the individual. The earlier the onset the greater the severity of impairment.

Mean IQ of persons with postnatal onset of epilepsy or acquiring it before age 4 was 87. The mean IQ of those individuals whose onset was between 5 and 9 years was 92. Subjects who manifest after age 10 obtained a mean IQ of 98, a value close to the population norm.

Duration

In adults, duration of the disease is negatively correlated with IQ.

Premorbid Intelligence

It has been noted that the premorbidly brighter individuals exhibit greater deterioration. Improvement in the clinical condition of the individual tends to retard the rate of deterioration.

Specific Psychological Deficits

Pattern analysis of WAIS subtests has not yielded a distribution of scores peculiar to individuals who have epilepsy.

There are, however, certain subtests which when ranked are found to be consistently high or low in the ordering. Therefore, Comprehension, Block Design and Object Assembly rank higher than Digit Span, Digit Symbol and

Arithmetic. This finding is in agreement with Dennerll (1964) who factor analyzed WAIS and WISC scores and observed that the Comprehension factor was performed better than an attention type of factor.

It has been previously documented by Fitzhugh, K., Fitzhugh, L.C. and Reitan, R. (1962) that cerebral impairment on the left side is manifested as a verbal deficit on the Wechsler scales, while performance deficits are lateralized to cerebral damage on the right side of the brain. Moreover, on several memory tasks, the left temporal lobe subjects exhibited impaired recall for verbal material while the right-sided individuals were deficient in the recall of non-verbal material.

Children and adults with centrencephalic epilepsy have been reported to be impaired on tasks that require sustained attention and concentration. Children with centrencephalic seizures have also been shown to be impaired in visual organizational abilities (Tarter, 1972).

Prior statements in this paper regarding test, re-test variability and skewedness toward lower IQ ranges in individuals who have epilepsy has been correlated with E.E.G. recordings during test performance. When an abnormal electrical discharge did occur, performance was markedly disrupted.

Hovey and Kooi (1955) have recorded the E.E.G. while administering test batteries. They found that a non-response of "don't know" occurred during paroxysmal E.E.G. activity. The authors interpret this finding as indicating a temporary loss of a goal idea during the paroxysmal burst.

Our data indicated that speed of access to information in short-term memory was sensitive to phenobarbital concentrations. Impairment of short-term memory may critically influence a person's ability to maintain attention, a crucial ability when one is trying to learn new information (MacLeod, Dekaban and Hunt, 1978).

EEG & IQ

There is strong empirical support for the notion that the type of E.E.G. abnormality is correlated with level of intellectual functioning (Collins and Lennox, 1960).

M. Seidenberg et al (1981) performed a study using adult out-patients who were evaluated on the WAIS. There were two groups the (SI) seizures improvement group and the (SU) seizures unimproved group. A number of conclusions can be made regarding the intellectual deterioration in epilepsy from these results. Those persons whose seizures decreased showed general test-re-test improvement. The reverse was true of the unimproved group. Second, test, re-test improvements occurred more frequently on the WAIS performance than the verbal measures. While the (SU) group showed little evidence of improvement, there also appeared to be little evidence of pronounced deterioration in their performance.

(Insert Table II here)

Stores (1973) and Hutt (1967) have shown that both clinical and sub-clinical, generalized spike-wave bursts can disrupt not only the registration of information but also its storage and recall and that these effects depend on the amount and complexity of the information as well as the rate at which the child works.

Lennox et al (1936) pointed out that the frequency of occurrence of seizure discharge is lessened by tasks requiring some degree of arousal. Above a certain level, however, the degree of attention becomes stressful, seizure discharge increases and performance declines.

It has been shown repeatedly (Dennerll, 1964; Milner, 1975; Cherlav and Serafetinides, 1976; Jones-Goternan, 1979) that temporal lobe epilepsy impairs memory functions. The left temporal lobe is specialized for learning and attention and the right temporal lobe for visuo-spatial and non-verbal material. Centrencephalic patients perform more poorly on tests of attention (Mirsky et

al, 1960). Cognitive abilities (Dikmen and Matthews, 1977) and long term memory (Ladavas et al, 1979) are significantly correlated negatively with duration of illness. An early age of onset of seizures is more apt to result in neuropsychological impairment (Dikmen, et al, 1975, 1977; O'Leary et al, 1981).

Learning

Holdsworth and Whitmore (1974a) studied a random group of children attending normal schools. Half of the children were achieving a very indifferent performance. In an earlier study (Whitmore and Holdsworth, 1971) of children with epilepsy, 42% were described as being "markedly inattentive". Stores and Hart (1976), in a study of factors associated with the progress of children with epilepsy attending normal classrooms, found that reading skills of those children taking phenytoin for at least two years were significantly inferior to those who had taken other anticonvulsant drugs over a similar period.

Stores (1975) points out many of the reports about adverse effects of drugs on learning are difficult to evaluate because they do not clearly distinguish between side effects, toxic effects, individual idiosyncrasy or do not give details of dosage and blood serum levels.

Although defects of attention are usually associated with subcortical seizure discharges, there is reason to suppose that frequently occurring localized cortical discharges may adversely affect some aspects of attention and learning. Studies of focal epilepsy suggest that when a part of the brain is occupied by an electrical discharge it cannot perform its normal functions. In general, it has been found that temporal lobe lesions in the hemisphere dominant for speech cause impairment of verbal abilities, including defects of retention and learning of verbal material, while lesions of the temporal lobe on the nondominant side tend to impair visuospatial skills and to cause perceptual

difficulties (Fedio and Mirsky, 1969; Ounsted, Lindsay and Norman, 1966).

Anticonvulsant Medications

Dosage, Therapeutic Range

Generic Name	Brand Name	Type of Seizure	Serum Level/Therapeutic Range
Phenytoin	Dilantin	Tonic-clonic/Complex partial	10-20 mg/L
Phenobarbital	----------	Tonic-clonic/Complex-partial Absence	10-50 mg/L
Valproic Acid	Depakene	Absence	50-100 mg/L
Primidone	Mysoline	Tonic-clonic/Focal/Complex partial	6-12 mg/L
Carbamazepine	Tegretol	Complex partial/Tonic-clonic	5-12 mg/L
Ethosuximide	Zarontin	Absence	50-100 mg/L
Clonazepam	Clonopin	Myoclonic/Absence	10-15 mg/L
Mephobarbital	Mebaril	Absence/Complex partial	----------
ACTH	Athar Gel	West's Syndrome(infantile spasms)	----------

Anticonvulsant Medications

Adverse Reactions

Anticonvulsant	Adverse Reactions
Dilantin	Nystagmus, ataxia, slurred speech, mental confusion, dizziness, insomnia, transient nervousness, motor twitchings, headaches, gingival hyperplasia.
Phenobarbital	Drowsiness, vertigo, headache, depression nausea, vomiting, diarrhea, hyperactivity.
Depakene	Nausea, vomiting, diarrhea, drowsiness, ataxia, depression, emotional upset, hepatic failure, non-specific symptoms such as; loss of seizure control, malaise, weakness, lethargy, anorexia.
Mysoline	Ataxia, vertigo, nausea, anorexia, vomitin fatigue, hyperirritability, emotional disturbances, impotency.
Tegretol	Dizziness, drowsiness, unsteady gait, nausea, vomiting, fever, dyspnea, frequent urination, urine retention, confusion, blood dyscrasias.
Zarontin	Anorexia, gastric upset, nausea, vomiting, drowsiness, headache, urticaria.

Anticonvulsant Medications

Adverse Reactions

Clonopin	Drowsiness, ataxia, behavior problems, abnormal eye movements.
Mebaril	Dizziness, headache, nausea, facial edema, skin rash.
Mesantoin	Blood dyscrasias, non-specific skin rashes, drowsiness, ataxia, fatigue, hyperirritability, depression, tremors.

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